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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/616,776	07/10/2003	Craig Heacock	CP241	1994

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EXAMINER	
AHMED, HASAN SYED	

ART UNIT	PAPER NUMBER
1615	

DATE MAILED: 04/19/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/616,776	HEACOCK ET AL.	
	Examiner	Art Unit	
	Hasan S. Ahmed	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 March 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *49-86 and 133-145* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *49-86 and 133-145* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Receipt is acknowledged of Applicant's letter filed on 30 January 2006, and response filed on 23 March 2006.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 49-86 and 133-145 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Grebow, et. al. (US 5,618,845).

Grebow, et. al. disclose a pharmaceutical composition comprising modafinil in particle form (col. 2, lines 6-8). The pharmaceutical composition may be used as a method of altering a somnolent state, such as narcolepsy, idiopathic hypersomnia, and other sleep disorders (col. 3, lines 56-58). The method involves administration to mammals of modafinil in particle form of a defined size (col. 3, lines 59-62). The reference indicates that an effective amount of the disclosed pharmaceutical composition is useful for enhancing alertness, or increasing regularity of sleep rhythms (col. 3, line 67 – col. 4, lines 1-3).

Grebow, et. al. employed several options to analyze modafinil particle size, i.e. laser diffraction particle size analysis, mechanical sieving, optical microscopy, ultracentrifugation, sedimentation, air permeability, electron microscopy, scanning electron microscopy and Coulter Counter techniques (col. 7, lines 33-38).

Grebow, et. al. teach that the size of the modafinil particles is important to the potency and safety profile of the drug (col. 2, lines 8-10). They (Grebow, et. al.) found at least two significant and unexpected advantages when administering modafinil in the form of particles of a defined size (col. 5, lines 21-23). First, they found increased potency of the drug; i.e. smaller average particle size allowed achievement of a set modafinil plasma concentration at a lower dose of the drug (col. 5, lines 23-25). Second, they explain that the safety profile of modafinil can be more accurately controlled because dosing with defined particle sizes proved to be reliable in achieving the desired plasma concentration of drug (col. 5, lines 25-31).

The Grebow, et. al. reference differs from the instant case only in that it does not specifically recognize about 10% of the total cumulative modafinil particles to by smaller than 25μm and about 5% of the total cumulative modafinil particles to be larger than 200μm. However, the particle sizes, including a particular combination, could be determined by one of ordinary skill in the art at the time of the invention, given the teachings in Grebow, et. al., i.e. a pharmaceutical composition of modafinil comprising distinct particle sizes, and the beneficial effects of such composition (see *supra*). Thus, there is no unexpected result in the two particle size combination of the instant case. The Grebow, et. al. reference uses the same drug as the instant case, to treat patients suffering from the same disease as the instant case, administered in the same way as the instant case, to give the same effect as the instant case.

Absent a showing of an unexpected result by the combination of particle sizes claimed in the instant case, it would be obvious to one of ordinary skill in the art to use

the claimed particle size combination of modafinil. The expected result would be treatment of narcolepsy, idiopathic hypersomnia, sleep apnea, and obstructive sleep apnea by enhancing alertness, or increasing regularity of sleep rhythms.

Response to Arguments

Applicants' arguments filed on 23 March 2006 have been fully considered but they are not persuasive.

Applicants argue that the Grebow reference teaches away from the instant invention because it discloses a lower percentage of "large" modafinil particles (diameter greater than 200 microns) than the instant invention.

Applicants' quote from mid-sentence of the text in col. 3, lines 16-20 of the Grebow reference implies that the Grebow reference sets 5% of the cumulative total of modafinil particles as a maximal limit of modafinil particles of diameter greater than 200 microns. However, a reading of the complete sentence reveals that Grebow has not set any brightline limitations; 5% is merely *preferable*.

Applicants cite the study at col. 8, line 53 – col. 9, line 36 of the Grebow reference to suggest that Grebow teaches away from using more than 5% cumulative total of modafinil particles greater than 200 microns. However, this study led Grebow to conclude that it is important to *control* modafinil particle sizes. No mention is made of the percentage of "large" modafinil particles having adverse side effects. Grebow states that

> [A] non-homogenous mixture of modafinil particle sizes may not provide consistent potency nor avoid undesired fluctuations in plasma modafinil

concentrations; such fluctuations can leasd to undesired and unexpected events. Moreover, the use of modafinil particles having defined size is more efficient because a given plasma modafinil concentrateion can be achieved at a lower oral dose. *See* col. 9, lines 39-47.

Applicants cite col. 4, line 53 – col. 5, line 21 of the Grebow reference to suggest that Grebow teaches that a formulation of more than 5% cumulative total of modafinil particles greater than 200 microns results lower potency than formulations with lower percentages of "large" modafinil particles. However, again, the Grebow reference discloses ranges, not brightline limitations. Grebow merely states that "smaller particle size" (*see* col. 5, line 17) results in increased potency of modafinil, without going into specific percentages. In fact, this conclusion of the Grebow reference is not inconsistent with the instant invention, which has a maximum limit of only 30% "large" modafinil particles; 70% or more of the modafinil particles of the instant invention are smaller than 200 microns in diamenter. Furthermore, Grebow suggests that the "early" lots containing a higher percentage of "large" modafinil particles had a better safety profile than "late" lots with a lower percentage of "large" modafinil particles (*see* col 4, lines 65-67).

Applicants suggest that the higher percentage of "large" modafinil particles in the instant invention are bioequivalent to the alleged lower percentage of modafinil particles in the Grebow reference. However, the specification does not provide any evidence for this conclusion. Applicant's specification (*see* page 10, paragraph 0104) states that a determination of bioequivalence requires "...extensive testing which includes

administering single doses of the test and reference drugs to a number of volunteers..." No such study is disclosed in the instant specification.

In fact, Applicants state in the specification that "it is to be expected that routine experimentation will be desirable to determine the optimum particle size makeup and proportions of blend mixtures that exhibit similar...bioequivalent to Provigil® (modafinil)." *See* page 6, paragraph 0064. The implication being that such studies have not been performed for the instant disclosure.

Attorney argument is not evidence unless it is an admission, in which case, an examiner may use the admission in making a rejection. *See* MPEP § 2129 and § 2144.03 for a discussion of admissions as prior art. The arguments of counsel cannot take the place of evidence in the record. *In re Schulze*, 346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA 1965); *In re Geisler*, 116 F.3d 1465, 43 USPQ2d 1362 (Fed. Cir. 1997) ("An assertion of what seems to follow from common experience is just attorney argument and not the kind of factual evidence that is required to rebut a prima facie case of obviousness."). *See* MPEP § 716.01(c) for examples of attorney statements which are not evidence and which must be supported by an appropriate affidavit or declaration.

Conclusion

Claims 49-86 and 133-145 remain rejected.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Hasan S. Ahmed whose telephone number is 571-272-4792. The examiner can normally be reached on 9am - 5:30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K. Page can be reached on 571-272-0602. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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